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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,803	11/14/2005	Giuseppe Arpaia	279737US0PCT	1463
22850	7590	05/21/2009	EXAMINER	
OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314			XU, XIAOYUN	
			ART UNIT	PAPER NUMBER
			1797	
			NOTIFICATION DATE	DELIVERY MODE
			05/21/2009	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com  
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jgardner@oblon.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/556,803	<b>Applicant(s)</b> ARPAIA ET AL.	
	<b>Examiner</b> ROBERT XU	<b>Art Unit</b> 1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 24 April 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 15-17 and 22-24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 15-17, 22-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### DETAILED ACTION

1. The amendment filed 04/24/2009 has been entered and fully considered. Claims 18-21 are canceled. Claims 15-17 and 22-24 are pending, of which Claim 15 is amended.

### *Response to Amendment*

2. In response to amendment, the examiner modifies rejection over the prior art established in the previous Office action.

### *Claim Rejections - 35 USC § 103*

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. **Claims 15 -17 and 22-23** are rejected under 35 U.S.C. 103(a) as being unpatentable over Katakam et al. (Pharmaceutical Development and Technology, 1997) (Katakam) in view of Wu (Journal of Endocrinology, 1993).

In regard to Claim 15, Katakam teaches the use of Poloxamer polymer to stabilize recombinant human growth hormone (rhGH) against various processing stress (see title). The method comprises:

mixing the protein sample (rhGH) by adding a Poloxamer to the sample (see page 144, right col., 3<sup>rd</sup> paragraph);

performing chromatography (size exclusion column- HPLC) on the protein sample (see page 145, right col. 1<sup>st</sup> paragraph); and

the quantity of the total protein is determined by UV absorbance of the eluted protein solution (see page 145, right col. 1<sup>st</sup> paragraph and Figure 1-2).

Katakam does not specifically teach using data from calibration with a standard to calculate the quantity of the protein. However, using data from calibration with a standard to calculate the quantity of the protein is well known in the art. At time of the invention, it would have been obvious for a person of ordinary skill in the art to use data from calibration with a standard to calculate the quantity of the protein.

Katakam does not teach FSH. Wu teaches that FSH from bovine pituitary glands is isolated by size exclusion (gel filtration) chromatography (see abstract). At the time of the invention, it would have been obvious to one of the ordinary skill in the art to add

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Poloxamer to the FSH sample for size exclusion chromatography to improve the yield, because Katakam teaches that Poloxamer polymer can stabilize protein against various processing stress.

In regard to Claim 16, simple dilution of protein sample to a level acceptable for the chromatographic system is well-known in the art.

In regard to Claim 17, Katakam teach using size-exclusion chromatography (SEC) to quantify protein (see page 145, right col. 1<sup>st</sup> paragraph).

In regard to Claim 22, Katakam teaches using Pluronic F68 to stabilize protein (Table 1).

In regard to Claim 23, Katakam tests various concentrations of Pluronic F68 in the range from 0.001% (below cmc) to 0.2% (above cmc) (see Table 1). The concentration of 100 µg/ml is equivalent to 0.01%. Katakam's teaching meets the recited limitation.

### ***Response to Arguments***

5. Applicant's arguments filed 04/24/2009 have been fully considered but they are not persuasive.

Applicants argue that there is no evidence cited in the rejection that supports the position that following what Katakam teaches, one of ordinary skill in the art would use a calibration curve. The court has held that the rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art, established scientific principles, or legal precedent established by prior case law. (see *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992)). In that regards, the knowledge of using calibration curve to quantify analysis result is established scientific principle and generally available to one of ordinary skill in the art. Therefore, it does not have to be expressly stated in Katakam.

Applicants argue that Katakam does not perform assessing the total quantity of the protein as defined in the claims. The chromatography method recited in the claim

can only quantify protein in the effluent buffer. Quantifying total protein means quantifying total protein in the effluent buffer. That is exactly what Katakam teaches.

Applicants argue that HGH and FSH are very different proteins, having remarkably different structures. Therefore, how one protein (HGH) acts in a given set of experiments (like in Katakam) provides no reasonable guidance as to how a second, distinct protein (FSH from Wu) would behave. Since Katakam demonstrates that Poloxamer reduces aggregation of HGH, it would have been obvious to one of ordinary skill in the art to apply the same method on other proteins. From particular to general is how science and engineering develop.

### ***Conclusion***

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT XU whose telephone number is (571)270-5560. The examiner can normally be reached on Mon-Thur 7:30am-5:00pm, Fri 7:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Kim can be reached on (571)272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

5/15/2009

/Yelena G. Gakh/  
Primary Examiner, Art Unit 1797

RX